

# MEDICATION SAFETY IN SECONDS

A MONTHLY PUBLICATION FROM VA MEDSAFE:  
VA'S COMPREHENSIVE PHARMACOVIGILANCE CENTER

## Helping to achieve safe medication use

### DIRECT ORAL ANTICOAGULANTS (DOAC)

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The Scientific and Standardization Committee (SSC) of the International Society of Hemostasis and Thrombosis (ISTH) recently published recommendations on the use of consistent nomenclature for the newer class of oral anticoagulants that directly inhibit a single target and have similar clinical properties (e.g., dabigatran, rivaroxaban, apixaban, and edoxaban). After evaluation of several possibilities, the SSC of the ISTH recommends **DOAC for direct oral anticoagulants**. The nomenclature has been endorsed by several professional societies including the Anticoagulation Forum. (*J Thromb Haemost. 2015;13:1154-6*)

VA had widely adopted the target specific oral anticoagulants or TSOAC nomenclature (e.g., PBM documents, policy, CPRS order-

ing menus, MUET, etc.) as was originally endorsed by the Anticoagulation Forum and VA subject matter experts. Based on the new ISTH recommendations, the MAP and VPEs (National PBM) agreed that VA should transition from TSOAC to DOAC to be consistent with practices outside of VA.

The field will begin to see the new nomenclature of DOAC in PBM documents, communications, policy, MUET, etc. Facilities are encouraged to re-evaluate local and VISN level use of the TSOAC term and consider transitioning to the DOAC term. It may be helpful to include a reference to the former name of TSOAC (e.g., Direct Oral Anticoagulant [DOAC], formerly called TSOAC).

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### VA PHARMACY BENEFITS MANAGEMENT SERVICES (PBM)

PBM maintains VA's national drug formulary, as well as promotes, optimizes, and assists VA practitioners with the safe and appropriate use of all medications.

### VA CENTER FOR MEDICATION SAFETY (VA MedSAFE)

VA MedSAFE performs pharmacovigilance activities; tracks adverse drug events (ADEs) using spontaneous and integrated databases; enhances education and communication of ADEs to the field; and promotes medication safety on a national level.

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## from the pbm

- Bactroban (Mupirocin) Recall: ADDENDUM – 12/17/2015 - [National PBM Patient Level Recall Communication](#)

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# from the fda

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## ENDOCRINOLOGY

### [FDA eliminates the Risk Evaluation and Mitigation Strategy \(REMS\) for rosiglitazone-containing diabetes medicines](#)

12/16/2015

FDA eliminates the Risk Evaluation and Mitigation Strategy (REMS) for rosiglitazone-containing type 2 diabetes agents (approved as Avandia, Avandamet, Avandaryl, and generics) as continued monitoring identified no new patient safety information. Data did not demonstrate an increased risk of heart attack with rosiglitazone compared to metformin and sulfonylurea. Manufacturers also satisfied requirements to provide educational training to health care professionals regarding cardiovascular risks of rosiglitazone medications.

### [FDA revises labels of SGLT2 inhibitors for diabetes to include warnings about too much acid in the blood and serious urinary tract infections](#)

12/04/2015

In May 2015, FDA warned that sodium-glucose cotransporter-2 (SGLT2) inhibitors for diabetes may result in high anion gap metabolic acidosis. In addition, PBM addressed this concern in a [National PBM Bulletin](#) around the same time. Since then, continuous evaluation of this safety issue has resulted in the addition of warnings to the labels of these agents for two safety issues: ketoacidosis as well as urinary tract infections, including urosepsis and pyelonephritis.

- FDA identified 73 cases of ketoacidosis associated with SGLT2 use reported to the FDA Adverse Event Reporting System (FAERS) from March 2013 until May 2015.
  - All cases were hospitalized or received treatment in the emergency room.
  - The median time from initiation of an SGLT2 inhibitor or an increase in dose to the onset of the reported ketoacidosis was 43 days (range 1 day to 1 year).
  - SGLT2 inhibitor was discontinued in 57 of the 73 cases.
  - Potential risk factors for developing ketoacidosis with an SGLT2 inhibitor identified in these cases include: infection, low carbohydrate diet or an overall reduction of caloric intake, reduction in or discontinuation of dose of exogenous insulin, discontinuation of oral insulin secretagogue, and alcohol use.
- FDA identified 19 cases of urosepsis associated with the use of SGLT2 inhibitors reported to FAERS from March 2013 through October 2014.
  - All cases resulted in hospitalization.
  - No deaths were reported.
  - The median time to onset was 45 days (range 2 to 270 days).
  - Discontinuation of the SGLT2 inhibitor was reported in 15 cases.

FDA recommends that health care providers:

#### For Ketoacidosis

- Be aware of the possible development of a high anion gap metabolic acidosis accompanied by elevation in urine or serum ketones associated with the use of SGLT2 inhibitors, even if glucose levels are not very high as is typical for DKA.
- Evaluate any presence of acidosis, including ketoacidosis, for appropriate action:
  - discontinue SGLT2 inhibitors if acidosis is confirmed;
  - correct the acidosis and monitor glucose levels;
  - treat and correct factors that may have precipitated or contributed to the metabolic acidosis.
- Educate patients and caregivers of the signs and symptoms of metabolic acidosis, such as tachypnea or hyperventilation, anorexia, abdominal pain, nausea, vomiting, lethargy, or mental status changes, and instruct them to seek medical attention immediately if these symptoms occur.

#### For Urosepsis and Pyelonephritis

- Evaluate patients for signs and symptoms of urinary tract infections;
- Treat promptly if indicated.

# Getting the most from our safety surveillance

## INTRALIPID I.V. FAT EMULSION PRODUCTS IN BIOFINE CONTAINERS: PARTICULATE MATTER OBSERVED

Baxter reports that small blue particulate matter has been observed during compounding with Intralipid I.V. Fat Emulsion 20% products in Biofine containers Fresenius Kabi (FK-Sweden). Table 1 lists affected product. Preliminary investigations reveal that the particulate matter in each case originated from the blue transfusion port when spiking the port at an angle. These complaints are associated with use of automated compounding sets. No adverse events have been reported. However, injection of a product containing particulate matter may block blood vessels, which may cause stroke, heart attack, or damage to other organs (i.e., kidney, lungs, liver). In addition, allergic reactions, local irritation, and inflammation in tissues and organs may occur. As such, Baxter recommends that health care professionals:

- *Should not use Intralipid in Biofine containers with automated compounding sets. Manual compounding and direct infusion sets can be continued.*
- *Examine the product carefully for particulate matter in a well-lit environment before infusing into a patient.*
- *Do not use the product if particulate matter is present.*
- *Use a 1.2 micron filter with Intralipid and admixtures containing Intralipid. Filters of less than 1.2 micron pore size must not be used.*
- *Follow the instructions for spiking as provided below:*
  - *Place the bag on a clean and flat surface;*
  - *Hold the base of the infusion port and insert the spike through the center of the septum by rotating the wrist slightly;*
  - *Assure that the spike is inserted straight into the port without an angle. ■*

Table 1. Affected Products.

PRODUCT CODE	DESCRIPTION	NDC	LOT NUMBER
2B6065	INTRALIPID®, 30% 500 ML	0338-0520-13	All Lot Numbers
2B6064	INTRALIPID®, 20% 1000 ML	0338-0519-14	All Lot Numbers
2B6063	INTRALIPID®, 20% 500 ML	0338-0519-13	All Lot Numbers
2B6062	INTRALIPID®, 20% 250 ML	0338-0519-12	All Lot Numbers
2B6061	INTRALIPID®, 20% 100 ML	0338-0519-58	All Lot Numbers